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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,340	04/01/2005	Robert Y.L. Tsai	4239-66642-05	5503

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EXAMINER	
PITRAK, JENNIFER S	

ART UNIT	PAPER NUMBER
1635	

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03/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,340	TSAI ET AL.	
	Examiner	Art Unit	
	JENNIFER PITRAK	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-54,56,61 and 64-76* is/are pending in the application.

4a) Of the above claim(s) *41,53,54,64 and 65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40, 42-52, 56, 61, 66-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/29/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Remarks

Applicant's claim amendments filed 12/23/2008 and arguments filed 08/29/2008 have been entered and considered. Claims 1-39, 55, 57-60, 62, and 63 are canceled. Claims 67-76 are new. Claims 40-54, 56, 61, and 64-76 are pending. Claims 41, 53, 54, 64, and 65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 03/18/2008. Claims 40, 42-52, 56, 61, and 66-76 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

In the response filed 12/23/2008, Applicant indicated concern that the supplemental IDS form PTO-1449 submitted 12/14/2005 (actually submitted 12/22/2005) had not been considered and has provided an additional copy of the PTO-1449 (08/29/2008). Applicant's attention is directed to the bottom of both IDS where it is indicated that all references have been considered unless lined through. All references on the 12/22/2005 and the 08/29/2008 IDS have been considered.

Claim Objections

Claims 40, 42-52, 56, 61, and 66-76 are objected to because of the following informalities:

Claim 51 reads in part "agent that identified as one". This is grammatically incorrect. Appropriate correction is required.

Claim Rejections - 35 USC § 112 - (Written Description) - Withdrawn

The rejection of claim 62 under 35 U.S.C. 112, first paragraph as failing to comply with the written description rejecition is withdrawn because the claim has been canceled.

Claim Rejections - 35 USC § 112 - (Written Description) - Maintained

Claims 40, 42-51, 56, 68-73, 75, and 76 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record.

Response to arguments

Applicant argues that the specification provides actual reduction to practice of several members of the genus of agents that alter the level of nucleostemin, including nucleic acids encoding nucleostemin and siRNAs, and that the specification also discloses several other members of the genus of agents and that such identified examples are sufficiently representative of the claimed genus so as to demonstrate adequate written description of the claimed invention (pages 8-9 of 08/29/2008 response). This is not persuasive for the reasons set forth in the rejection, namely that the claimed genus is very large and varied (see page 3 of 05/29/2008 Office Action), and because the specification only contemplates the agents other than nucleic acids encoding nucleostemin and siRNAs. Furthermore, the claims requiring the use of siRNAs

or any other agent are not specific to nucleostemin-targeted agents, but include those that indirectly alter nucleostemin levels (see page 3 of 05/29/2008 Office Action).

Applicant also argues that the amendments to the claims limiting the nucleostemin polypeptide amino acid sequences to those having 95% identity to the reference sequence and requiring the functions of the reference polypeptide would allow a person of ordinary skill in the art to envision the entire scope of the claimed invention. This is not persuasive for the reasons set forth in the preceding paragraph. However, in light of the specification as indicated in Applicant's arguments, it is acknowledged that one of ordinary skill in the art would know or be able to determine what sequences having 95% identity to SEQ ID NO:10 or to SEQ ID NO:6 would also have preserved nucleostemin function.

Claim Rejections - 35 USC § 112 - (Enablement) - Withdrawn

The rejection of claims 57-60 and 62 under 35 U.S.C. 112, first paragraph, as lacking enablement is withdrawn because the claims have been canceled.

Claim Rejections - 35 USC § 112 - (Enablement) - Maintained

Claims 40, 42-52, 56, 61, 66-76 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing senescence in cells *in vitro* by administration of a nucleostemin-targeted siRNA, does not reasonably provide enablement for inducing senescence in any cell type by administering any agent that may increase or decrease nucleostemin protein levels. The specification does not enable one of skill in the art to induce senescence of cells *in vivo* by any means. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the

invention commensurate in scope with these claims. This rejection is maintained for the reasons of record.

Response to arguments

Applicant argues that undue experimentation is not required to determine in what cell types senescence may be induced *in vitro* by modulation of nucleostemin levels because those of skill in the art can readily isolate and experiment with different cell types. This is not persuasive. The fact that with a given agent, one of skill in the art can screen various cells *in vitro* for the induction of senescence is not contested. What is at issue is the scope of the agents encompassed by the claims as described in the written description rejection. Undue experimentation is required to determine which of all possible agents will induce senescence *in vitro*.

Applicant argues that *in vivo* induction of cell senescence is enabled by the art and presents three references published more than 4 years after the filing date of the instant application in support of Applicant's argument. This is not persuasive. Enablement of Applicant's invention must be evident at the time of filing. Applicant's arguments with regard to siRNA therapy are not persuasive because, although the Nguyen reference (cited in the 05/29/2008 Office Action) pertaining to siRNA delivery addresses therapeutic uses of siRNAs, the reference is primarily relied upon to demonstrate that even in 2008, *in vivo* delivery of siRNAs is still problematic and is limited to direct delivery to target organs and tissues (see page 7 of 05/29/2008 Office Action). Given the scope of the claims and the disclosure of the specification, the instant claims are clearly not enabled for *in vivo* methods.

Claim Rejections - 35 USC § 102 - Withdrawn

The rejection of claim 56-58 and 62 under 35 U.S.C. 102(e) as being anticipated by Kennedy, et al. (2003/0008284, of record) is withdrawn because the amendments to the claims have obviated the rejection.

Claim Rejections - 35 USC § 102 - Maintained

Claims 40, 42, 43, and 46-51 are rejected under 35 U.S.C. 102(e) as being anticipated by Kennedy, et al. (2003/0008284, of record). This rejection is maintained for the reasons of record.

Response to arguments

Applicant argues that the claims as amended to include the feature of "determining senescence of the cell" is not anticipated by Kennedy because Kennedy does not teach the step of determining senescence. This is not persuasive. Although Kennedy does not explicitly claim "determining senescence", Kennedy teaches and claims a method of inhibiting tumor growth. Inhibiting tumor growth involves a lack of cell division, which by definition is senescence. The step of determing senescence is implicit in Kennedy's step of inhibiting tumor growth.

Claim Rejections - 35 USC § 103 - Withdrawn

The rejection of claims 57, 58, and 62 under 35 U.S.C. 103(a) as being unpatentable over Kennedy are withdrawn because the claim amendments have obviated the rejection.

The rejection of claim 66 under 35 U.S.C. 103(a) as being unpatentable over Kennedy and Bass is withdrawn because the claim amendments have obviated the rejection.

Claim Rejections - 35 USC § 103 - Maintained

Claims 40, 42-51, and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kennedy. This rejection is maintained for the reasons of record. Regarding amended claim 56, this claim would have been obvious to one of skill in the art because one of skill would recognize that the claimed *in vitro* methods could be achieved in CNS stem cells because Kennedy teaches the use of stem cells and any necessary experimentation to test induced senescence in particular stem cell types is merely routine, and thus not undue.

Response to arguments

Applicant argues that claims are not obvious over Kennedy because the limitation, "determining senescence of the cell" in the amended claim 40 is not taught by Kennedy. This is not persuasive for the reasons set forth above in the response to arguments to the rejection under 35 U.S.C. 102(e).

Applicant further argues that the claims would not be obvious over Kennedy because the teachings of Kennedy provide no expectation of success. Applicant points to Example 8 of Kennedy and interprets the example to indicate that only one antisense oligonucleotide inhibited cell proliferation and that the example teaches that a reduction of nucleostemin has no effect on cell proliferation or induction of senescence (page 15 of Applicant's 08/29/2008 response). This is not persuasive. Example 8 simply does not show the results of antisense inhibition of nucleostemin, which is not evidence that antisense inhibition of nucleostemin does not induce senescence. Kennedy teaches or renders obvious all of the claimed method steps of inhibiting nucleostemin and, absent evidence to the contrary, such steps are appropriately assumed to achieve the claimed result of inducing senescence.

Claims 40, 42-52, 56, 61, 68-73, 75, and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kennedy as applied to claims 40, 42-51, and 56 above, and further in view of Bass (2001, Nature v.411:428-9, of record). This rejection is maintained for the reasons of record.

Response to arguments

Applicant argues that Bass does not overcome the deficiencies of Kennedy because Bass makes no mention of senescence. This is not persuasive because the Bass reference is relied upon to teach siRNAs, which Bass indicates as performing better than antisense oligonucleotides at inhibiting target gene expression.

Allowable Subject Matter

SEQ ID NO: 7 is free of the prior art searched.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak
Examiner
Art Unit 1635

/Tracy Vivlemore/
Primary Examiner, Art Unit 1635